

REMARKS**Rejection of Claims and Traversal Thereof**

In the February 4, 2008 Office Action:

claims 27, 28, and 30-33 were rejected under 35 U.S.C. §102(e) as being anticipated by Balloul et al. (US Patent No. 7,354,591, hereinafter Balloul);

claims 29, 34-40 and 48 were rejected under 35 U.S.C. §103(a) as being unpatentable over Balloul in further view of Harris, et al. (International Immunology, 1997, Vol 9, p 273-280).

These rejections are hereby traversed and reconsideration of the patentability of the pending claims is therefore requested in light of the following remarks.

Rejection under 35 U.S.C. §102(e)

Claims 27, 28, and 30-33 were rejected under 35 U.S.C. §102(e) as being anticipated by Balloul et al. Applicants insist that Balloul is not an anticipatory reference and does not defeat the patentability of the claimed invention.

Applicants' claim 27 recites:

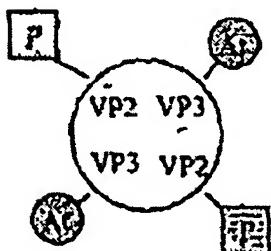
A method of producing a recombinant virus-like particle that targets specific tissue in a target animal, the method comprising:

- (a) providing a viral genome;
- (b) isolating viral coat protein sequences that encode for a capsid structure;
- (c) inserting at least one first exogenous sequence encoding a protein or peptide of interest into the coat protein sequences, wherein the protein or peptide is antigenic or allergen in the target animal;
- (d) inserting at least one second exogenous sequence encoding a tissue-targeting protein sequence in the animal into the coat protein sequences, wherein the expressed targeting protein has affinity for a receptor on tissue in the target animal;
- (e) cloning the viral coat protein sequences comprising the first and second exogenous sequences into an appropriate vector; and
- (f) transforming a yeast, bacterial or algae host organism for expression of the recombinant virus-like particle.

Anticipation under 35 U.S.C. § 102 requires the presence in a single reference of each and every element of the claimed invention, **arranged as in the claim**. *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984) (emphasis added)

Figure 1 of the present application, recreated below for ease of discussion, shows the elements of applicants' invention, wherein capsid proteins are recombinantly modified to include two separate and distinct sequences. One of the sequences express antigenic or allergenic proteins (At) for display on the outer surface of the capsid and the second sequence encodes for a tissue-targeting protein (P) which is also exposed on the surface. Thus importantly the capsid is a delivery device that has two additional proteins displayed on the surface that are not normally displayed on such a capsid.

Importantly the tissue-targeting protein (P) helps target the antigen (At) to the cell surface, such as intestinal mucosa. Thus, the present invention provides for three separate and distinct expressed components, the capsid protein with both the antigen protein and the tissue target protein displayed on the surface as shown below.



Applicants insist that the Balloul reference does not in any way disclose, teach or suggest the presently claimed invention. Applicants have reviewed the entire Balloul and the reference does not in any way describe the presentation or display of two exogenous proteins on the surface of the virus capsid.

Balloul teaches the use of poxviral particle having on its surface a heterologous ligand moiety that has specificity and ability to bind to a binding ligand on the targeted cell. Thus it is important to recognize that Balloul has a ligand moiety on the capsid surface that has a corresponding anti-ligand binding receptor on the target cell. Reviewing column 4, of Balloul, it is evident that there is just one exogenous sequence (or termed heterologous ligand moiety) that encodes for ligand that binds to an anti-ligand molecule that is localized at the surface of the target cell.

The present invention concerns a poxviral particle having a targeted infection specificity towards target cells wherein said particle infects preferably said target cells and wherein said specificity is conferred by at least one heterologous ligand moiety which is localized at the surface of said poxviral particle and which is capable of binding an anti-ligand molecule localized at the surface of said target cells, with the proviso that when said poxviral particle is an EEV vaccinia virus particle said ligand is not an antibody directed to ErbB-2.

Notably there is no mention of a second exogenous sequence that encodes for an antigen or allergen. There is no discussion in Balloul for any sequence that does not have a corresponding binding site on the target tissue. This is discussed in column 5 of Balloul as shown below:

In general, the ligand moieties that may be used in the context of the present invention are widely described in the literature: it is a moiety able to confer to the modified poxviral particle of the invention, the ability to bind to a given anti-ligand molecule or a class of anti-ligand molecules localized at the surface of at least one target cell.

Further there is a discussion at column 6 wherein the ligand is an antibody that binds to an anti-ligand receptor on the cell which is an antigen.

In one preferred embodiment, the anti-ligand molecule is an antigen (e.g. a cell-specific antigen, a disease-specific antigen, an antigen specifically expressed on the surface of engineered target cells, . . .) and the ligand moiety is an antibody, a fragment or a minimal recognition unit thereof (i.e. a fragment still presenting an antigenic specificity) such as those described in detail in immunology manuals (see for example Immunology, third edition 1993, Rott, Brostoff and Male, ed Gambli, Mosby). The ligand moiety may be a monoclonal antibody. Monoclonal antibodies which will

In Example 5 of Balloul, the results show that only a single ligand was expressed on the surface, as shown below:

All together, these results indicate that the ligand moiety SM3 scFv is expressed at the surface of the poxviral (IMV) particles and that it is capable of recognizing and binding to its target (the MUC-1 antigen) leading to a specific infection of said cells by the modified virus.

It is clear, as shown above, that in the Balloul reference there is absolutely no discussion for two separate and different proteins expressed on the surface.

In contrast, the present invention included a capsid with two unrelated proteins, not only to each other but also the capsid, wherein one of the expressed proteins has a binding site on the target tissue and the antigen or allergen does not require such a binding site.

Further it should be noted that the Balloul reference does not in any way discuss the transforming of a yeast, bacterial or algae host organism for expression of the recombinant virus-like particle. Instead the expression of the poxviral particle is expressed in chicken embryo fibroblasts (CEF) as described in column 17, lines 17 to 40. Further discussion relating to the use of CEF cells can be found in Example 1, section C of Balloul. Applicants agree that some markers from *e coli* were used in the plasmids for isolation of the end product but applicants could not locate any text in Balloul wherein the host cell was a yeast, bacterial or algae cell.

Clearly, there is no disclosure for a virus capsid that displays two different and separate exogenous proteins as described in applicants' claimed invention and there is no indication that a yeast, bacteria or algae host cell was used as culturing cells. Thus, Balloul does not anticipate the presently claimed invention and applicants request that this rejection under section 102 be withdrawn.

Rejection under 35 U.S.C. §103(a)

Claims 29, 34-40 and 48 were rejected under 35 U.S.C. §103(a) as being unpatentable over Balloul in further view of Harris. Applicants insist that the proposed combination does not in any way render the presently claimed invention as obvious.

Clearly, the Balloul reference does not in any way disclose, teach or suggest all the claimed elements of the presently claimed invention and the addition of Harris does not rectify such shortcomings especially because Harris teaches the use of only a single allergen that has affinity for a CD8 cell surface receptor.

According to the Office, one skilled in the art would consider combining the technology of Harris and Balloul because Harris teaches an allergen and Balloul teaches a targeting ligand. However, applicants disagree because there is the problem that both of these references teach only a single protein on the surface of the expressed particle. Further it is important to recognize that both of these references teach

that the specific expressed proteins are used to targeting the expressed particle to a specific receptor location on tissue. Thus each expressed protein has its own distinct landing site.

Thus, if you combine the two references you will have introduced a “tug-of-war” between the two expressed proteins and this battle will be won by the protein with stronger affinity for its binding site. As such, there is a very good chance that one of the surface proteins will not operate as intended. According to the court in *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984), if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification and the Office has not established a *prima facie* case of obviousness.

In conclusion, the proposed combination of Balloul and Harris does not disclose, teach or suggest all the claimed limitations of the presently claimed invention and if combined will no longer function as intended. In light of the above discussion, applicants submit that the Office has not established a *prima facie* case of obviousness, and as such, applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

Rejoining of Withdrawn Claims

Applicants request that method claims 41 to 47 be rejoined when the product claims are found allowable.

Fees payable

It is believed that no fees are due at this time. However, if a fee is found due, the Commissioner is hereby authorized to charge any deficiencies, or reimburse any over-charges, to Deposit Account No. 13-4365 of Moore & Van Allen, PLLC.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Boesen reconsider the patentability of the pending in light of the distinguishing remarks herein, and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly

solicited. In the event that any issues remain, Examiner Boesen is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,



Marianne Fuierer
Reg. No. 39,983
Attorney for Applicants

Moore & Van Allen, PLLC
Telephone: (919) 286-8000
Facsimile: (919) 286-8199